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(54) A multilayer laminated blister film

Ein Blisterfilm aus Multischichtslaminat

Un film de type blister à couches laminées multiples

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EP 0 646 367 B1

Description

This invention relates generally to the field of manufacturing and dispensing pharmaceuticals, and more particularly to a blister film for use in the manufacture and packaging of pharmaceutical tablets. Particularly, it relates to a laminated blister film for use in blister packs.

In recent years, pharmaceutical producers have turned to the use of blister packs for use in both the forming and dispensing of pharmaceutical tablets. These blister packs generally consist of a blister sheet or blister film and a lidding sheet. The blister sheet contains depressions for containing individual dosages. In a standard process for manufacturing freeze dried tablets, a single dosage, in liquid form, is introduced into each depression of the blister sheet. The blister sheet, along with the liquid dosages, is then placed into a refrigerated environment where the dosages are subjected to low temperatures to freeze them. The blister sheets are then transferred to a freeze drier, where the ice is removed by sublimation. When freeze drying is completed, the sheets are removed from the drying chamber and covered with an adhesive lidding sheet, which seals the solid dosages into their individual depressions. US Patent No. 4,305,502 teaches inter alia, a known process for manufacturing freeze dried tablets.

Blister sheets that have heretofore been used in freezing and freeze drying processes have suffered from several deficiencies. First, the blister sheets have typically been made of a polymeric substance, which, over time, can allow moisture to permeate the blister pack and reach the dosages stored inside. To solve this problem, blister sheets have been developed in which a layer of aluminum is laminated between layers of polymer. While the presence of the aluminum layer prevents moisture from permeating the blister pack, it leads to a second problem. When subjected to temperature changes during the freezing process, conventional aluminum/polymer laminates tend to curl up, due to the differences in the degree of thermal expansion or contraction of the opposing layers of the laminate. This makes their use in freezing processes difficult, since liquid product can easily spill from the formed depressions or can lie unevenly in the depressions during filling and freezing operations. Furthermore, the curling of the blister sheet can cause dosages to freeze or sublimate unevenly, since some depressions may not be in physical contact with the cold surfaces of the refrigerator or freeze drier. The only solution has been to use weights on the edges of the laminate strips to hold them sufficiently flat. Such measures are not practical in large scale manufacturing operations, and can interfere with the freezing process.

The present invention is directed at a multilayer laminated blister film comprising an impermeable intermediate layer (normally of aluminum) positioned between first and second outer layers. The film is formed with a plurality of individual depressions for receiving liquid dosages. According to the invention the first and second outer layers have substantially similar coefficients of thermal expansion. At least one of the outer layers is usually a polymeric substance, and both may be made of the same substance and/or have substantially the same thickness.

The properties of the outer layers in laminates of the invention are such that there are no inter-layer stresses that will cause curvature of the laminate when it is subjected to temperature changes during the freeze drying process. The symmetrical response of the outer layers to such temperature changes can be achieved by using the same film material for both outer layers, or by using different materials which by virtue of their intrinsic properties or thickness, exhibit similar degrees of thermal expansion or contraction. The outer layers can each consist of separate sublayers, as long as the sublayers in one outer layer are such that the outer layer, as a whole exhibits the same overall degree of expansion or contraction as the other outer layer. Following the introduction of the dosages into the depressions of the blister sheet, the dosages are frozen and freeze dried. A lidding sheet is then attached to the blister sheet to seal the solid dosages into the blister pack.

The invention will now be described by way of example and with reference to the accompanying drawings, wherein:

Figure 1 is a plan view of a blister sheet, showing the configuration of dosage depressions therein;

Figure 2 is a transverse cross sectional view of the blister pack of Figure 1, taken on line 2--2;

Figure 3 is a cross sectional view of a blister sheet according to a first embodiment of the invention, illustrating the relationship between its intermediate and outer layers;

Figure 4 is a cross sectional view of a blister sheet according to a second embodiment of the invention illustrating the relationship between its various layers and sublayers; and

Figure 5 is a cross sectional view of a blister pack with the lidding sheet in place.

As shown in Figures 1 and 2 a blister sheet comprises a strip 12 of the desired laminate formed with depressions 10 through conventional cold forming. The size and shape of the depressions is a matter of choice that will be dictated by the size and nature of the tablet to be formed, as well as other considerations that are well known to those persons skilled in the art.

Turning to Figure 3, the laminate strip 12 comprises an intermediate layer 14 that is substantially impermeable to moisture. The preferred material for the intermediate layer is aluminum having a thickness of 10 to 100 µm, with the preferred thickness being approximately 45 µm, although other suitable materials may be used in its

place. The intermediate aluminum layer 14 is sandwiched between a first outer layer 16 and a second outer layer 18. The outer layers may be coated or laminated onto the intermediate layer, but the layers do not necessarily have to be bonded together. The first and second outer layers are preferably made of polymeric substances, including polyamide, polyvinylchloride, polypropylene or other such substances. The first and second outer layers can be made of the same or different materials, and may have different thicknesses, as long as they have substantially similar coefficients of thermal expansion, i.e. are made of such materials and have such thickness that the first and second outer layers exhibit substantially the same degree of expansion or contraction within the plane of the film when the laminate is subjected to changes in temperature, particularly within the range of temperatures encountered during the freezing process, in which temperatures can be as low as -196°C. For instance, the laminated film 12 can consist of an intermediate layer 14 of aluminum, positioned between first and second outer layers of polypropylene 16 and 18, each layer being approximately 50 µm thick.

Turning to Figure 4, it can be seen that one or both of the outer layers can also consist of separate sublayers, with each sublayer being either polymeric or non-polymeric.

For instance, the first outer layer 16 can consist of two or more sublayers, such as a polyamide sublayer 20 and a polyvinylchloride sublayer 22. The second outer layer 18 can consist of identical sublayers, or can also consist of two or more sublayers, illustrated as 24, 26 and 28, that are different than the sublayers in the first outer layer 16. Materials that may be used as sublayers include the above mentioned polymers, as well as lacquer, aluminum or paper. A priming layer can also be included. Again, the primary concern is that the first outer layer 16 and the second outer layer 18 exhibit, overall, substantially the same degree of expansion or contraction in response to temperature changes, so as to prevent curling of the blister sheet.

In a freeze drying process using a blister sheet as described above, a single dosage 30 of pharmaceutical, in liquid form, is introduced into each depression 10 of the strip 12 in a conventional manner. The blister sheet is then placed into a refrigeration unit, for instance a nitrogen spray freezing chamber, where both the sheet and the dosages are subjected to temperatures sufficient to rapidly freeze the dosages, typically as low as -196°C. Once the dosages have frozen, the blister sheet is transferred to a freeze drying chamber. Within the freeze drying chamber, the dosages are subjected to a vacuum of typically 0.1 to 1.0 mBar for a period of 180 to 500 minutes. At the same time, the temperature is steadily increased from typically about -30°C to about 60°C. Once the dosages have been freeze dried, an adhesive lidding sheet 32 is positioned over the blister sheet, sealing the dosages into the individual depressions of the blister sheet. The procedures associated with the introduction of dosages into the blister sheet, the freezing and freeze drying of the dosages and the attachment of the lidding sheet are known to persons of skill in the art, and need not be treated in great depth herein.

Claims

1. A multilayer laminated blister film (12) comprising an impermeable intermediate layer (14) positioned between first and second outer layers (16, 18) with a plurality of individual depressions (10) therein for receiving liquid dosages,
   CHARACTERISED IN THAT
   the first and second outer layers (16, 18) have substantially similar coefficients of thermal expansion.

2. A blister film according to Claim 1, wherein the intermediate layer (14) of the blister film is aluminum.

3. A blister film according to Claim 1 or Claim 2, wherein the outer layers (16, 18) of the blister film are made of the same substances.

4. A blister film according to any preceding Claim, wherein at least one of the outer layers (16, 18) of the blister film is a polymeric substance.

5. A blister film according to Claim 4, wherein the polymeric substance comprises at least one polymer selected from the group consisting of polyethylene, polyamide, polyvinylchloride and polypropylene.

6. A blister film according to any preceding Claim, wherein the outer layers (16, 18) of the blister film have substantially the same thickness.

7. A blister film according to any preceding Claim, wherein at least one of the outer layers (16, 18) of the blister film further comprises a plurality of sublayers (20, 22, 24, 26, 28).

8. A blister film according to Claim 7, wherein one of the sublayers is a lacquer or priming layer.

9. A blister film according to Claim 7 or Claim 8, wherein one of the sublayers is a polymeric substance.

10. A blister film according to Claim 9, wherein the polymeric substance comprises one or more polymers selected from the group consisting of polyethylene, polyamide, polyvinylchloride and polypropylene.

Patentansprüche

1. Blisterfilm aus Multischichtlaminat (12), der eine undurchlässige Zwischenschicht (14) aufweist, die

zwischen ersten und äußeren Schichten (16, 18) angeordnet ist, und mit einer Mehrzahl von individuellen Vertiefungen (10) darin zur Aufnahme von flüssigen Dosiereinheiten, **dadurch gekennzeichnet, daß**
die ersten und zweiten äußeren Schichten (16, 18) im wesentlichen gleiche thermische Ausdehnungskoeffizienten besitzen.

2. Blisterfilm nach Anspruch 1, dadurch gekennzeichnet, daß die Zwischenschicht (14) des Blisterfilms aus Aluminium besteht.

3. Blisterfilm nach Anspruch 1 oder 2, dadurch gekennzeichnet, daß die äußeren Schichten (16, 18) des Blisterfilms aus den gleichen Materialien hergestellt sind.

4. Blisterfilm nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, daß zumindest eine der äußeren Schichten (16, 18) des Blisterfilms aus einem Polymer-Material hergestellt ist.

5. Blisterfilm nach Anspruch 4, dadurch gekennzeichnet, daß das Polymer-Material zumindest ein Polymer aufweist, das aus der aus Polyäthylen, Polyamid, Polyvenylchlorid und Polypropylen bestehenden Gruppe ausgewählt ist.

6. Blisterfilm nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, daß die äußeren Schichten (16, 18) des Blisterfilms im wesentlichen die gleiche Dicke aufweisen.

7. Blisterfilm nach einem der vorstehenden Ansprüche, dadurch gekennzeichnet, daß zumindest eine der äußeren Schichten (16, 18) des Blisterfilms weiterhin eine Mehrzahl von Teilschichten (20, 22, 24, 26, 28) aufweist.

8. Blisterfilm nach Anspruch 7, dadurch gekennzeichnet, daß eine der Teilschichten eine Lack- oder Grundierungsschicht ist.

9. Blisterfilm nach Anspruch 7 oder 8, dadurch gekennzeichnet, daß eine der Teilschichten eine polymere Substanz ist.

10. Blisterfilm nach Anspruch 9, dadurch gekennzeichnet, daß die polymere Substanz ein oder mehrere Polymere aufweist, die aus der aus Polyäthylen, Polyamid, Polyvenylchlorid und Polypropylen bestehenden Gruppe ausgewählt sind.

Revendications

1. Film à bulles, à couches laminées multiples (12), comprenant une couche intermédiaire imperméable (14) positionnée entre des première et seconde couches extérieures (16, 18) avec une pluralité de creux individuels (10) dans celui-ci destinés à recevoir des doses liquides,
CARACTERISE EN CE QUE
les première et seconde couches extérieures (16, 18) présentent des coefficients de dilatation thermique sensiblement similaires.

2. Film à bulles selon la revendication 1, dans lequel la couche intermédiaire (14) du film à bulles est en aluminium.

3. Film à bulles selon la revendication 1 ou la revendication 2, dans lequel les couches extérieures (16, 18) du film à bulles sont faites des mêmes substances.

4. Film à bulles selon l'une quelconque des revendications précédentes dans lequel au moins une des couches extérieures (16, 18) du film à bulles est une substance polymère.

5. Film à bulles selon la revendication 4, dans lequel la substance polymère comprend au moins un polymère choisi parmi le groupe constitué du polyéthylène, du polyamide, du chlorure de polyvinyle et du polypropylène.

6. Film à bulles selon l'une quelconque des revendications précédentes, dans lequel les couches extérieures (16, 18) du film à bulles présentent sensiblement la même épaisseur.

7. Film à bulles selon l'une quelconque des revendications précédentes, dans lequel au moins une des couches extérieures (16, 18) du film à bulles comprend en outre une pluralité de sous-couches (20, 22, 24, 26, 28).

8. Film à bulles selon la revendication 7, dans lequel l'une des sous-couches est une laque ou une couche d'apprêt.

9. Film à bulles selon la revendication 7 ou la revendication 8, dans lequel l'une des sous-couches est une substance polymère.

10. Film à bulles selon la revendication 9, dans lequel la substance polymère comprend un ou plusieurs polymères choisis parmi le groupe constitué du polyéthylène, du polyamide, du chlorure de polyvinyle et du polypropylène.

Fig.1

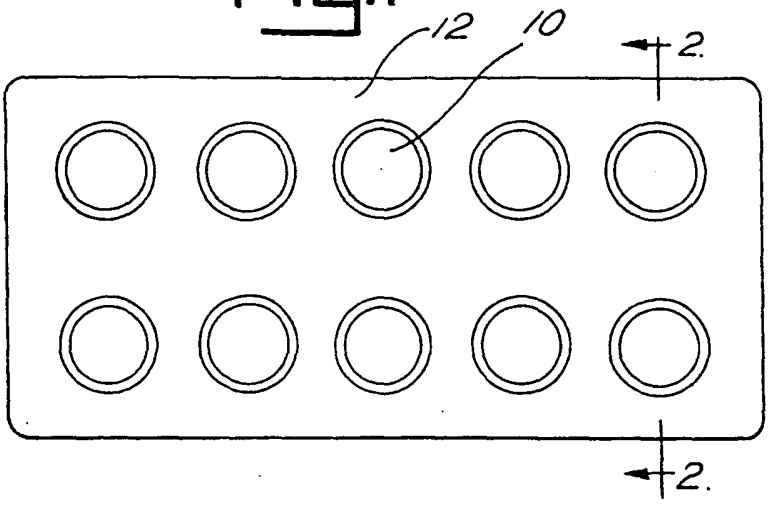

Fig.2

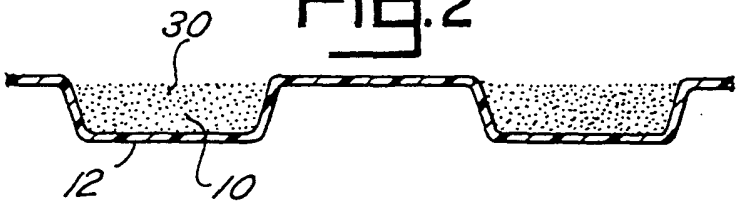

Fig.3

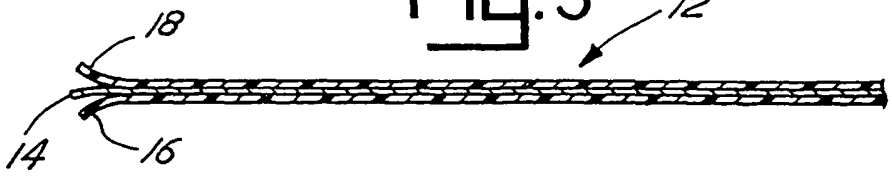

Fig.4

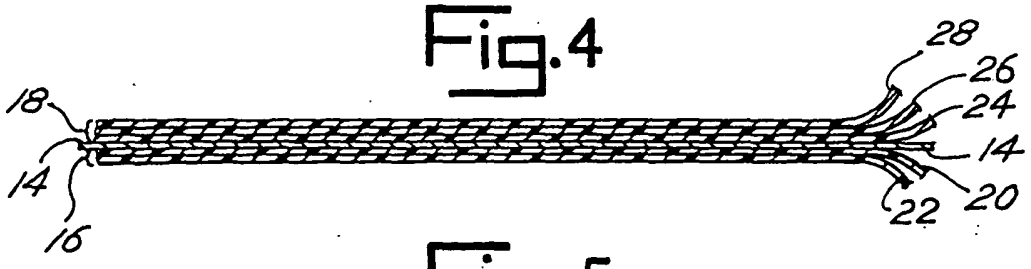

Fig.5